

**AMENDMENTS TO THE CLAIMS:**

This listing of claims will replace prior versions and listings of claims in the application:

**Listing of claims:**

Claims 30, 31, 46, 47, 51, 52, 53, 55, 56, 59, 60, 65, 67 and 92-109 have been amended as follows: Underlines indicate insertions and ~~striketrough~~ indicate deletions. Claims 38, 66, 68 and 74 were cancelled. Previously withdrawn claims 50, 61-64, 84-91 and 110-113 were also cancelled while retaining the right to resubmit them in a divisional application.

1-29. (Cancelled)

30. (Currently amended) A soluble polypeptide of a subtilisin-kexin isoenzyme (SKI-1), ~~named SKI-1 which has~~ the amino acid sequence ~~defined by~~ of which consists of amino acids 187 to 996 of SEQ ID NO: 6~~7~~.

31. (Currently amended) A polypeptide of a subtilisin-kexin isoenzyme (SKI-1), ~~named SKI-1, which has~~ the amino acid sequence ~~defined by~~ of which consists of amino acids 17 to 137 of SEQ ID NO: 6, which is capable of binding with amino acids 17 to 1052 of SKI-1.

32. (Previously presented) The polypeptide of claim 31, wherein said polypeptide has a molecular weight of about 14 kDa when resolved by SDS-PAGE on a 8% gel and forms a complex with the soluble fragment of SKI-1.

33. (cancelled)

34. (cancelled)

35. (cancelled)

36. (Previously presented) An isolated nucleic acid encoding a polypeptide as defined in claim 30.

37. (Previously presented) An isolated nucleic acid encoding a polypeptide as defined in claim 31.

38. (cancelled)

39. (cancelled)

40. (Previously presented) A recombinant vector comprising the nucleic acid defined in claim 36.

41. (Previously presented) The recombinant vector of claim 40, which is an expression vector.

42. (Previously presented) The recombinant vector of claim 41, which comprises a promoter expressible in a target cell wherein expression of said nucleic acid is desirable.

43. (Previously presented) The recombinant vector of claim 42, which comprises an inducible promoter.

44. (Previously presented) A recombinant host cell comprising the recombinant vector defined in claim 40.

45. (Previously presented) A method of producing a fragment of SKI-1 enzyme, which comprises the steps of:

culturing a recombinant host cell expressing a nucleic acid as defined in claim 36 in an expression-supportive culture medium; and recovering said fragment of SKI-1 in the culture medium.

46. (Currently amended) A method for cleaving a substrate for a SKI-1 enzyme, which comprises the step of:

a) ~~contacting said substrate with~~ 1) a soluble fragment of a subtilisin-kexin isoenzyme, ~~which has the amino acid sequence of which consists of defined by~~ amino acids 187-996 of SEQ ID NO: 6, ~~—~~; 2) a catalytic part of 1); ~~or~~ 3) a complex as defined in claim 32, for a time sufficient and in conditions adequate for such cleavage to occur, whereby cleavage of the substrate occurs;

with the proviso that said substrate is not a sterol-regulatory element-binding protein (SREBP) ~~and is not SKI-1.~~

47. (Currently amended) A method for producing a protein or a peptide from a precursor which is an enzymatic substrate for a SKI-1 enzyme, which comprises the steps of:

a) contacting said ~~proteie~~ precursor with 1) a soluble fragment of a subtilisin-kexin isoenzyme, ~~which has the amino acid sequence of which consists of defined by~~ amino acids 187-996 of ~~any one of~~ SEQ ID NO: 6, ~~—~~; ~~or~~ 2) a catalytic part of 1) ~~—~~; ~~or~~ 3) a complex as defined in claim 32, for a time sufficient and in conditions adequate for such cleavage to occur; and

b) recovering said protein or peptide;

with the proviso that said substrate is not a sterol-regulatory element-binding protein (SREBP) ~~and is not SKI-1.~~

48. (Previously presented) The method of claim 47, which takes place in a cell or in the presence of a cellular population and wherein step a) comprises the step of transfecting a cell with a nucleic acid expressing said SKI-1 enzyme.

49. (Previously presented) The method of claim 48, wherein said cell expresses said precursor or is transfected with a nucleic acid expressing said precursor.

50. (Cancelled)

51. (Currently amended) A peptide of ~~at least~~ between 7 and 13 amino acids capable of binding to, and of being cleaved by, a SKI-1 catalytic site, said peptide comprising a sequence as set forth in any one of SEQ ID NO: 7, SEQ ID NO: 9 and SEQ ID NO: 11,

with the proviso that said peptide does not comprise the sequence as set forth in SEQ ID NO: 78 and with the proviso that said substrate is not a sterol-regulatory element-binding protein (SREBP) ~~or a part thereof or SKI-1 or a part thereof.~~

52. (Currently amended) A peptide as defined in claim 51, wherein said peptide comprises the sequence as set forth in any one of SEQ ID NO: 8, SEQ ID NO: 10 and SEQ ID NO: 12.

53. (Currently amended) A peptide as defined in claim ~~52~~ 51 which comprises the sequence+ as set forth in SEQ ID NO: ~~77~~ 13.

54. (Previously presented) A peptide as defined in claim 51 which is labelled.

55. (Currently amended) A peptide as defined in claim ~~54~~ 51 which is fluorogenic.

56. (Currently amended) A peptide as defined in claim ~~55~~ 51, the amino acid sequence of which consists of the sequence as set forth in SEQ ID NO: 14. ~~which is Abz-SEQ ID NO: 77-  
Tyr(NO<sub>2</sub>)<sub>7</sub>  
wherein Abz is orthoaminobenzoic acid, and Tyr(NO<sub>2</sub>) is 3-nitrotyrosine.~~

57-58. (Cancelled)

59. (Currently amended) A method for screening for a polypeptide that has the activity of a subtilisin-kexin isoenzyme (SKI-1) ~~named SKI-1~~, the method comprising the steps of:

contacting the peptide of claim 51 ~~to~~ with a test polypeptide under conditions that allow cleavage of the peptide by a the SKI-1; and

detecting the cleavage of the peptide wherein the presence of the cleavage indicates that the polypeptide has SKI-1 activity.

60. (Currently amended) A method for monitoring the activity of a subtilisin-kexin isoenzyme (SKI-1) ~~named SKI-1~~ comprising the steps of:

contacting a sample having or suspected of having SKI-1 activity with the peptide of claim 51; and  
monitoring the cleavage of the peptide.

61. (Cancelled)

62. (Cancelled)

63. (Cancelled)

64. (Cancelled)

65. (Currently amended) A composition comprising a soluble polypeptide of a SKI-1 fragment as defined in claim 30.

66. (Cancelled)

67. (Currently amended) A composition comprising a polypeptide of a SKI-1 fragment as defined in claim 31.

68. (cancelled)

69. (cancelled)

70. (cancelled)

71. (cancelled)

72. (Previously presented) A composition comprising a nucleic acid as defined in claim 36.

73. (Previously presented) A composition comprising a nucleic acid as defined in claim 37.

74. (cancelled)

75-79. (Cancelled)

80. (Previously presented) A composition comprising a recombinant vector as defined in claim 40.

81. (Previously presented) A composition comprising a recombinant vector as defined in claim 41.

82. (Previously presented) A composition comprising a recombinant vector as defined in claim 42.

83. (Previously presented) A composition comprising a recombinant vector as defined in claim 43.

84. (Cancelled)

85. (Cancelled)

86. (Cancelled)

87. (Cancelled)

88. (Cancelled)

89. (Cancelled)

90. (Cancelled)

91. (Cancelled)

92. (Currently amended) A purified polypeptide, the amino acid sequence of which consists of ~~defined by~~ amino acids 1 to 188 of SEQ ID NO: 6.

93. (Currently amended) A purified polypeptide, the amino acid sequence of which consists of ~~defined by~~ amino acids 1 to 197 of SEQ ID NO: 6.

94. (Currently amended) A purified polypeptide, the amino acid sequence of which consists of ~~defined by~~ amino acids 1 to 169 of SEQ ID NO: 6.

95. (Currently amended) A purified polypeptide, the amino acid sequence of which consists of ~~defined by~~ amino acids 17 to 188 of SEQ ID NO: 6.

96. (Currently amended) A purified polypeptide, the amino acid sequence of which consists of ~~defined by~~ amino acids 17 to 197 of SEQ ID NO: 6.

97. (Currently amended) A purified polypeptide, the amino acid sequence of which consists of ~~defined by~~ amino acids 17 to 169 of SEQ ID NO: 6.

98. (Currently amended) An isolated nucleic acid encoding a the polypeptide ~~as defined in~~ of claim 92.

99. (Currently amended) An isolated nucleic acid encoding a the polypeptide ~~as defined in~~ of claim 93.

100. (Currently amended) An isolated nucleic acid encoding a the polypeptide ~~as defined in~~ of claim 94.

101. (Currently amended) An isolated nucleic acid encoding a the polypeptide ~~as defined in~~ of claim 95.



102. (Currently amended) An isolated nucleic acid ~~comprising a sequence that encodes~~ encoding the a polypeptide ~~as defined in~~ of claim 96.

103. (Currently amended) An isolated nucleic acid encoding a the polypeptide ~~as defined in~~ of claim 97.

104. (Currently amended) A composition comprising a the polypeptide ~~as defined in~~ of claim 92.

105. (Currently amended) A composition comprising a the polypeptide ~~as defined in~~ of claim 93.

106. (Currently amended) A composition comprising a the polypeptide ~~as defined in~~ of claim 94.

107. (Currently amended) A composition comprising a the polypeptide ~~as defined in~~ of claim 95.

108. (Currently amended) A composition comprising a the polypeptide ~~as defined in~~ of claim 96.

109. (Currently amended) A composition comprising a the polypeptide ~~as defined in~~ of claim 97.

110. (Cancelled)

111. (Cancelled)

112. (Cancelled)

113. (Cancelled)

114. (Previously presented) A recombinant vector comprising the isolated nucleic acid defined in claim 98.

115. (Previously presented) A recombinant vector comprising the isolated nucleic acid defined in claim 99.

116. (Previously presented) A recombinant vector comprising the isolated nucleic acid defined in claim 100.

117. (Previously presented) A recombinant vector comprising the isolated nucleic acid defined in claim 101.

118. (Previously presented) A recombinant vector comprising the isolated nucleic acid defined in claim 102.

119. (Previously presented) A recombinant vector comprising the isolated nucleic acid defined in claim 103.